PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB2005/001243	29.03.2005	25.03.2004

International Patent Classification (IPC) or both national classification and IPC
A61M31/00, A61M25/10

Applicant
HYDRODYNAMIC GENE DELIVERY LTD

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/GB2005/001243

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1,3-5,9,20

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 1,3-5,9,20

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	10,11,19
	No:	Claims	2,6-8,12-18
Inventive step (IS)	Yes:	Claims	
	No:	Claims	2,6-8,10-19
Industrial applicability (IA)	Yes:	Claims	2,6-8,10-19
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

see form 210

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:
   D1: US-A-5 922 687 (MANN ET AL) 13 July 1999
   D2: US-B1-6 494 861 (TSUKERNIK VLADIMIR) 17 December 2002
   D3: US 2004/253212 A1 (KOIWAI KAZUNORI ET AL) 16 December 2004
   D4: US-B1-6 685 672 (FORMAN MICHAEL ROBERT) 3 February 2004
   D5: US-A-5 411 479 (BODDEN ET AL) 2 May 1995
   D6: US 2001/041865 A1 (DELANEY DAVE ET AL) 15 November 2001

2. The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 2, 6, 7, 8, 12 to 18 is not new in the sense of Article 33(2) PCT.

2.1 The document D1 discloses in fig. 5B in combination with figures 1A-1C an apparatus for introducing nucleic acid into cells of a region of the body comprising the following features (the references in parentheses applying to this document):
- a reservoir (10) for holding a liquid formulation which comprises said nucleic acid;
- a catheter tube (550,560) in fluid communication with said reservoir for conveying said liquid formulation to said body region via an efferent vessel (512,514) of said body region (524; see fig. 5b; col. 8, lines 21-23);
- pressure development means (12) for pressurising the liquid conveyed by the catheter;
- occlusion means (552, 562) for substantially occluding said efferent vessel.

It is considered that the same pressure development means shown in fig. 1A-1C (or 5A) are also used in the embodiment of figure 5B. No other pressure developing means is mentioned in the document, so that it is inherent that the same means as in figure 1 are also used in the other embodiments

Since all features of claim 1 are anticipated by the apparatus known from D1, the requirement of novelty is not met.

2.2 It is noted that the embodiment in figure 4A, 4B in combination with fig. 1A-C of D1 also anticipates the subject-matter of claim 1.

2.3 The apparatus of D1 anticipates also the subject-matter of the following claims:

claim 6: see col. 2, lines 52-57;
claim 7: see col. 14, lines 15-23;
claim 8: see fig. 5B, one bailoon; see fig. 4B, two balloons are disclosed;
claim 12, 13:
see fig. 1, at least one syringe is also used with the embodiment in fig. 5B;
claim 14: see fig. 4B;
claim 15-18:
implicit in fig. 5B, since two lumen must be there for inflation and drug delivery; also it is normal to use the drug delivery lumen (which is in fig. 5B the central lumen) also for the guidewire.

3. The subject-matter of claim 2 is also anticipated by the devices disclosed in documents D2, and D4 to D6, see the relevant passages cited in the search report. It is noted that document D4 is not explicitly relating to the delivery of nucleic acids, but since the claim only defines that the apparatus must be suitable for such a use (see PCT Guidelines Chapter 5.23), and further since the liquid is not defined as one of its features, and since the device in D4 has all features which render it clearly suitable for the intended use, this prior art document is considered to be novelty destroying. For a similar reason also the devices of documents D5 and D6 anticipate the subject-matter of claim 2.

4. Dependent claims 10, 11 and 19 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step, the reasons being as follows:

The additional features defined in claims 10, 11 and 19 relate to configurations which come within the scope of the customary practice followed by persons skilled in the art, especially as the advantages thus achieved can readily be foreseen. Consequently, the subject-matter of these claims lacks an inventive step.

Re Item VI
Certain published documents cited

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
US-A-2004/253212	16.12.2004	7.5.2004	16.5.2003

The apparatus disclosed in figure 1 appears to anticipate the subject-matter of at least claims 2, 7, 8, 12, 13 and 15-18.

Re Item VII
Certain defects in the international application

1. The claims are not provided with reference signs, contrary to Rule 6. 2(b) PCT.

2. The independent claim is not in two-part form, contrary to Rule 6.3(b) PCT.

3. The prior art known from documents D1, D2, D4, D5, D6 is not acknowledged in the description, contrary to Rule 6.1(a)(ii) PCT.

Re Item VIII
Certain observations on the international application

1. The subject-matter of claim 6 lacks clarity (Art. 6 PCT), because it only indicates a result to be achieved without defining the necessary structural features. For the assessment of novelty and inventive step such a feature is not suitable to properly distinguish the subject-matter over the prior art.

2. The subject-matter of claims 10 and 11 lacks clarity, since it relates to the total volume of liquid formulation, but leaving it open which structural features are implied. Does it mean that the reservoir should be limited to such a volume, are there more than one reservoir ? Or is this only an indication of how much shall be introduced during the execution of the therapy, hence defining a limitation only for a method but

not for an apparatus. For the assessment of novelty and inventive step such a feature is not suitable to properly distinguish the subject-matter over the prior art.